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09/203,500	12/01/1998	KONRAD HONOLD	P564-8025	4303

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EXAMINER	
SANDALS, WILLIAM O	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/203,500	Applicant(s) Honold et al.
	Examiner William Sandals	Art Unit 1636

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 12, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *20-43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *41-43* is/are allowed.

6) ☒ Claim(s) *20-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☒ Interview Summary (PTO-413) Paper No(s). 26
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Response to Arguments

1. Amendments to the claims in Paper No. 24, filed December 12, 2001 have overcome the rejection of the claims under 35 USC 112, second paragraph in the previous office action, and the rejection is withdrawn.

2. Arguments filed in Paper No. 24 regarding the rejection of claims 41-43 under 35 USC 103(a) over US 6,020,144 and Cruz et al. have been fully considered and found persuasive, since claims 41-43 are drawn to a mammalian cell. The rejection is withdrawn for claims 41-43. However, the rejection for claims 36-40 is not found persuasive and the rejection is sustained. The response to the arguments is contained in the rejection repeated below.

3. Arguments filed in Paper No. 24 regarding the rejection of the claims under 35 USC 102(e) and 103(a) have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

Specification

5. The disclosure is objected to because of the following informalities: The section of the specification from page 41 to page 51 is configured to resemble the claims, while it is clearly

headed by a statement that it is intended to be part of the description. The format is easily misconstrued to be claimed subject matter. This being the case, the specification is confusing and unclear. Rearranging the text of pages 41-51, such that the format does not look like a claims set would cure this defect. This could be effected by deleting the numbering of the sentences, for example.

This problem was discussed in a conversation with Mr. Dan Dzara on April 15, 2002.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 20-25, 28-31, 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 20 recites at section" (i)" "at least one sequence, which upon expression is capable of changing the expression of the nucleic acid sequence which is present endogenously in the cell, and selected from the group consisting of a heterologous expression control sequence and an amplification gene", which is followed at section "(d)" which states "expressing the at least one

sequence". An expression control sequence is not capable of being expressed, therefore, the claim is vague and indefinite.

9. Claim 20 recites at section "(d)" "expressing the at least one sequence of (i) to thereby change the expression of the nucleic acid sequence which is present endogenously in the cell". No method step is recited to show how the expression of the "at least one sequence of (i)" will affect the expression of the nucleic acid sequence which is present endogenously in the cell. Therefore, the claim is vague and indefinite.

10. Claim 24 recites at section" (i)" "at least one sequence selected from the group consisting of a heterologous expression control sequence and an amplification gene each of which upon expression is capable of changing the expression of the nucleic acid sequence which is present endogenously in the cell". An expression control sequence is not capable of being expressed, therefore, the claim is vague and indefinite.

11. Claim 25 recites at section" (i)"" "at least one sequence selected from the group consisting of a heterologous expression control sequence and an amplification gene each of which upon expression is capable of changing the expression of the nucleic acid sequence which is present endogenously in the cell". An expression control sequence is not capable of being expressed, therefore, the claim is vague and indefinite.

12. Claim 27 recites at section "(d)" "expressing the at least one sequence of (i) under conditions under which the activator protein is bound thereby changing the expression of the nucleic acid sequence which is present endogenously in the cell". No method step is recited to

show how the expression of the "at least one sequence of (i)" will affect the expression of the nucleic acid sequence which is present endogenously in the cell. Therefore, the claim is vague and indefinite.

13. Claim 35 recites at the preamble a "process for testing the influence of non-coding nucleic acid sequences from the region of a target gene present endogenously in a eukaryotic cell on its expression". Section "(ii)" states that the vector of section "(a)" contains non-coding sequences from the 5' or 3' region of the target gene, then at section "(c)" claim 35 recites "measuring expression of the reporter gene". No method step is present in the claim which connects the presence of the non-coding sequences in the vector with the expression of the reporter gene. The claim is therefore vague and indefinite.

14. Claim 35 is rejected as being incomplete for omitting an essential step, such omission does not set forth the method in clear and unambiguous terms. See MPEP § 2172.01. The omitted step is a correlation, or recapitulation step at the end of the claim which restates the preamble, otherwise the claims do not result in what is stated in the preamble.

15. Claim 36 recites at section "(i)" "at least one DHFR-negative target sequence for a site-specific recombinase". No definition or explanation is provided as to what is meant by "at least one DHFR-negative target sequence for a site-specific recombinase". The meaning of the phrase is not an art recognized phrase, and would not be understood by a skilled artisan. The claim is therefore vague and indefinite.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

17. Claims 25-27, 32-35 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 5,695,977.

US Pat No. 5,695,977 taught (see especially the abstract and columns 2-8) a vector comprising an amplification gene sequence (DHFR), or a nucleic acid which binds an activator protein, and a selectable marker flanked by recombinase target sequences which may have a negative selection marker outside the recombinase target sequences. The vector may be inserted adjacent to an endogenous gene. The vector may be present in a human cell. Also taught is a process for testing the action of the amplification gene sequence or a nucleic acid which binds an activator protein on the expression of an endogenous target gene.

Response to Arguments

18. Arguments set forth in Paper No. 24 assert that the teachings of US 5,695,977 "merely recites a 'laundry list' of possible elements to be used in the art of homologous recombination", and that US 5,695,977 never contemplated the arrangement of the instant invention. On the contrary, US 5,695,977 makes a diligent effort to set forth the many possible configurations of

their inventive concept. The alleged "laundry list" is instead a description of the options available to one of ordinary skill in the art for the practice of the invention of US 5,695,977. Homologous recombination of a construct for the insertion of desired sequences into a target site, is a preferred method. The construct is recited to contain sequences encoding a marker, an expression control sequence, an amplification sequence, which may be DHFR, and these sequences may be inserted into the target DNA with flanking recombinase target sequences, so that the inserted sequence may be removed, or conversely, so that a sequence may be inserted at the site of the recombinase target sequences. The insert sequences are recited to influence the expression of endogenous genes, such as genes which result in genetic defects or which control metabolic pathways, as well as regulation of transcription and translation.

19. It is further argued in Paper No. 24 that the arrangement of the limitations as set forth in the claims are not anticipated by US 5,695,977. The arrangement of the limitations of US 5,695,977 is presented in such a way as to allow multiple configurations. This flexibility of the limitations of US 5,695,977 provides a broad scope of teachings. This broad scope of teachings is presented with sufficient diligence to anticipate the arrangement of elements as contemplated in the instant claimed invention.

20. Arguments set forth in Paper No. 24 assert that US 5,695,977 taught that the integration may occur with little preference for the site of integration. At column 4, lines 27-40 US 5,695,977 teaches the construct may be inserted at a desired site of integration.

21. It is argued in Paper No. 24 that the instant claimed invention teaches activation of endogenous genes. No such claim limitations are found in the claims, making the argument moot.

22. Paper No. 24 asserts that US 5,695,977 does not teach the use of recombinase recognition sequences as disclosed in the instant application. US 5,695,977 taught the use of flanking recombination sequences in combination with the desired sequence to facilitate insertion and deletion of sequences after they have been integrated into the target DNA site by homologous recombination. This meets the limitations of the claims.

23. It is asserted that there is no teaching to use recombination sequences in combination with amplification genes. Amplification genes are taught by US 5,695,977 as being a desirable element which may be carried in the construct to the desired site by the homologous recombination sequences which flank it. Recombinase sites are taught as useful to flank the desirable element (such as an amplification gene) to facilitate insertion and deletion of the desirable element once it is integrated into the target DNA.

24. Paper No. 24 asserts that US 5,695,977 teaches a "two step process" which involves tandem multicopy recombination recognition sequences. This element in the teachings of US 5,695,977 is but one of the embodiments associated with the use of recombinase recognition sequences, and is not the exclusive use of recombinase recognition sequences. The argument is therefore not found convincing.

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. Claims 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,020,144 in view of Cruz et al. (PNAS, Vol. 88, 1991).

The claims are drawn to a process for obtaining a DHFR-negative eukaryotic cell by transfecting the cell with a first vector comprising at least one target sequence for a site-specific recombinase, homologous DHFR DNA sequences which flank the recombinase site-specific sequence(s) and an optional positive selection marker gene and an optional negative selection marker gene. Transfecting the vector in the cell whereby homologous recombination occurs causing the vector to insert in the genome of the cell to produce a DHFR-negative cell. The claims are also drawn to a process for producing a eukaryotic cell which has been transfected with a vector which introduced a heterologous DHFR gene into the genome of the DHFR-negative cell by homologous recombination.

US Pat No. 6,020,144 taught (see especially columns 5, 15 and example 2) a process for obtaining a DHFR-negative trypanosomal cell by transfecting the cell with a first vector comprising at least one target sequence for a site-specific recombinase, homologous DHFR DNA sequences which flank the recombinase site-specific sequence(s) and an optional positive

selection marker gene and an optional negative selection marker gene. Transfecting the vector in the cell whereby homologous recombination occurs causing the vector to insert in the genome of the cell to produce a DHFR-negative trypanosomal eukaryotic cell. US Pat No. 6,020,144 also taught a process for producing a trypanosomal cell which has been transfected with a vector which introduced a heterologous DHFR gene into the genome of the DHFR-negative cell by homologous recombination.

Cruz et al. taught (see especially the abstract) the deletion of DHFR and subsequent replacement with a heterologous DHFR in a cell.

It would have been obvious to one of skill in the art at the time of filing the instant application to combine a process for obtaining a DHFR-negative eukaryotic cell by transfecting the cell with a first vector comprising at least one target sequence for a site-specific recombinase, homologous DHFR DNA sequences which flank the recombinase site-specific sequence(s) and an optional positive selection marker gene and an optional negative selection marker gene, then transfecting the vector in the cell whereby homologous recombination occurs causing the vector to insert in the genome of the cell to produce a DHFR-negative trypanosomal eukaryotic cell. Also taught was a process for producing a trypanosomal cell which has been transfected with a vector which introduced a heterologous DHFR gene into the genome of the DHFR-negative cell by homologous recombination of US Pat No. 6,020,144 with the process of deletion of DHFR and subsequent replacement with a heterologous DHFR in a eukaryotic cell as taught by Cruz et

al. because both US Pat No. 6,020,144 and Cruz et al. were investigating the replacement of DHFR in a trypanosomal cell with a heterologous DHFR.

One of skill in the art would have been motivated at the time of filing the instant application to combine a process for obtaining a DHFR-negative eukaryotic cell by transfecting the cell with a first vector comprising at least one target sequence for a site-specific recombinase, homologous DHFR DNA sequences which flank the recombinase site-specific sequence(s) and an optional positive selection marker gene and an optional negative selection marker gene, then transfecting the vector in the cell whereby homologous recombination occurs causing the vector to insert in the genome of the cell to produce a DHFR-negative trypanosomal eukaryotic cell. Also taught was a process for producing a trypanosomal cell which has been transfected with a vector which introduced a heterologous DHFR gene into the genome of the DHFR-negative cell by homologous recombination of US Pat No. 6,020,144 with the process of deletion of DHFR and subsequent replacement with a heterologous DHFR in a cell as taught by Cruz et al. because both US Pat No. 6,020,144 and Cruz et al. taught the desirable and beneficial replacement of DHFR in a DHFR- eukaryotic cell with a heterologous DHFR. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US Pat No. 6,020,144 and Cruz et al.

Response to Arguments

27. Paper No. 24 asserts that Cruz et al. did not discuss the preparation of recombinant proteins. The claims are not drawn to this limitation, therefore the argument is moot.

28. Paper No. 24 asserts that Cruz et al. requires two steps, wherein the instant invention only requires one step. The method of Cruz et al. requires one step to introduce the DHFR- ts gene into the target genome by homologous recombination. Therefore, the argument is not found convincing.

29. Paper No. 24 asserts that the transposon technique of US 6,020,144 is not the same as a recombinase technique as claimed, and challenges this examiner's assertion that a transposon technique is equivalent to a recombinase technique. US 5,434,066 teaches at columns 4-7, especially at column 6, line 53 bridging to column 7, line 18, that transposons are known as site-specific recombinases.

30. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, US 6,020,144 and Cruz et al. were both investigating the creation of DHFR- cells and used slightly different methods to achieve the same result. It is obvious to combine the method steps of two teachings reciting a common purpose in similar methods.

31. Claims 20-28 and 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364.

The claims are drawn to the invention as described in the rejection above, and where the vector comprises at least one nucleic acid which binds an activator protein.

US Pat No. 5,965,977 taught the invention as described above.

US Pat No. 5,695,977 did not teach a vector which comprises at least one nucleic acid which binds an activator protein which is a heterologous control sequence.

US Pat No. 6,130,364 taught (see especially the abstract and columns 11-12, 13,16-17 and 21) a process for introducing a vector by homologous recombination adjacent to a target gene, where the vector comprised at least one nucleic acid which binds an activator protein which is a heterologous control sequence which is flanked by recombinase target sites which is in turn flanked by sequences which target the vector to insert by homologous recombination at a site adjacent to a target gene.

WO 94/12650 taught (see especially the abstract and pages 2-5 and 16-23 and example 6) a process for introducing a vector by homologous recombination adjacent to a target gene, where the vector comprised at least one nucleic acid which binds an activator protein which is a heterologous control sequence which is flanked by recombinase target sites which is in turn flanked by sequences which target the vector to insert by homologous recombination at a site adjacent to a target gene.

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the vector comprising an amplification gene sequence (DHFR), or a nucleic acid which binds an activator protein, and a selectable marker flanked by recombinase target sequences which may have a negative selection marker outside the recombinase target sequences. The vector may be inserted adjacent to an endogenous gene. The vector may be present in a human cell. Also taught is a process for testing the action of the amplification gene sequence or a nucleic acid which binds an activator protein on the expression of an endogenous target gene as taught by US Pat No. 5,695,977 with the process for introducing a vector by homologous recombination adjacent to a target gene, where the vector comprised at least one nucleic acid which binds an activator protein which is a heterologous control sequence which is flanked by recombinase target sites which is in turn flanked by sequences which target the vector to insert by homologous recombination at a site adjacent to a target gene of WO 94/12650 and US Pat No. 6,130,364 because the nucleic acid which binds an activator protein and the amplification sequence are both taught as equivalents by WO 94/12650.

One of ordinary skill in the art would have been motivated at the time of filing of the instant application to combine the vector comprising an amplification gene sequence (DHFR), or a nucleic acid which binds an activator protein, and a selectable marker flanked by recombinase target sequences which may have a negative selection marker outside the recombinase target sequences. The vector may be inserted adjacent to an endogenous gene. The vector may be present in a human cell. Also taught is a process for testing the action of the amplification gene

sequence or a nucleic acid which binds an activator protein on the expression of an endogenous target gene as taught by US Pat No. 5,695,977 with the process for introducing a vector by homologous recombination adjacent to a target gene, where the vector comprised at least one nucleic acid which binds an activator protein which is a heterologous control sequence which is flanked by recombinase target sites which is in turn flanked by sequences which target the vector to insert by homologous recombination at a site adjacent to a target gene of WO 94/12650 and US Pat No. 6,130,364 because WO 94/12650 taught at page 22, line 29 bridging to page 23, line 2 "targeting sequences - DNA encoding an amplifiable positively selectable marker - DNA encoding a second selectable marker (optional) - DNA sequences corresponding to either an exogenous gene to be expressed under the control of a suitable promoter or a promoter only which is positioned to activate an endogenous gene - targeting DNA sequences." Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US Pat No. 5,695,977 with WO 94/12650 and US Pat No. 6,130,364.

Response to Arguments

32. Paper No. 24 asserts that US 6,130,364 teaches a two step process for inserting a desired sequence into a target DNA, where the homologous recombination occurs first, followed by insertion of a recombinase recognition site. At column 12, US 6,130,364 recites a "homology-targeting vector" which contains the desired sequence flanked by the recombinase recognition

sites which are flanked by the homologous recombination sequences. This "homology-targeting vector" is then inserted in one step into the target DNA.

33. Paper No. 24 asserts that WO 94/12650 does not teach site-specific recombination sequences. At pages 12, 13 and 72 WO 94/12650 teaches the inclusion of retroviral LTR's in the construct. Retroviral LTR's are known to contain target sequences for a retrotransposon, which is a site-specific recombinase, and is stated in WO 94/12650 that these LTR sequences can mediate excision of a desired sequence (which occurs via the recombinase mechanism).

34. Claims 20-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 as applied to claims 20-28 and 30-35 above, and further in view of WO 97/37012.

The claims are drawn to the invention as described above and to hypoxia-inducible factor-binding nucleic acid sequence.

5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 taught the invention as described above.

5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 did not teach that the vector comprised at least one nucleic acid which binds an activator protein which was a hypoxia-inducible factor-binding nucleic acid sequence.

WO 97/37012 taught (see especially pages 11-12) a vector which introduced control sequences adjacent to a target gene by homologous recombination where the control sequence was a hypoxia-inducible factor-binding nucleic acid sequence.

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the invention of US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 as described above with the vector which comprised at least one nucleic acid which binds an activator protein which was a hypoxia-inducible factor-binding nucleic acid sequence of WO 97/37012 because WO 97/37012 taught the equivalence of the vector which comprised at least one nucleic acid which binds an activator protein of US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 with a vector which comprised at least one nucleic acid which binds an activator protein which was a hypoxia-inducible factor-binding nucleic acid sequence.

One of ordinary skill in the art would have been motivated at the time of filing of the instant application to combine the invention of US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364 as described above with the vector which comprised at least one nucleic acid which binds an activator protein which was a hypoxia-inducible factor-binding nucleic acid sequence of WO 97/37012 because WO 97/37012 taught at page 11, line 22 bridging to page 12, line 5 "[e]xamples of preferred promoters....heat shock or other environmentally-inducible promoter such as those induced by anaerobiosis or hypoxia". Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the

producing the instant claimed invention given the teachings of US Pat No. 5,695,977 in view of WO 94/12650 and US Pat No. 6,130,364, and further in view of WO 97/37012.

Response to Arguments

35. Paper No. 24 asserts that WO 97/37012 taught only the insertion of an HIF binding sequence in a target nucleic acid by homologous recombination. WO 97/37012 was used to demonstrate the well known and obvious inclusion of the HIF binding sequence in a construct for the purposes of producing an inducible promoter. US 5,695,977 taught the desirable and useful inclusion of inducible promoters in the construct. The argument is therefore not found convincing.

Allowable Subject Matter

36. Claims 41-43 are allowed.

Conclusion

37. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

38. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.
Examiner
April 17, 2002

TERRY MCKELVEY
PRIMARY EXAMINER